



NUTRITION THERAPY FOR WOUNDS

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Disclosure

- The content of this program has met the continuing education criteria of being evidence-based, fair and balanced, and non-promotional.
- This educational event is supported by Abbott Nutrition Health Institute, Abbott Nutrition.
- Dr. Sherry is an Employee of Abbott Nutrition

Learning Objectives

- Describe the process of wound healing requirements for macro-and micronutrients
- Review the nutrition care process for individuals at risk and experiencing wound healing
- Learn nutrition interventions to augment wound healing

Introduction

This presentation reviews complexities associated with wound care and best practices to eliminate and overcome barriers of effective care through nutrition. The process and progress of wound healing with nutrition as a vital component is addressed, including particular nutrient requirements

Wound Incidence/Prevalence

About 2% of the U.S. adult population has a chronic wound.

- Chronic wounds are considered:

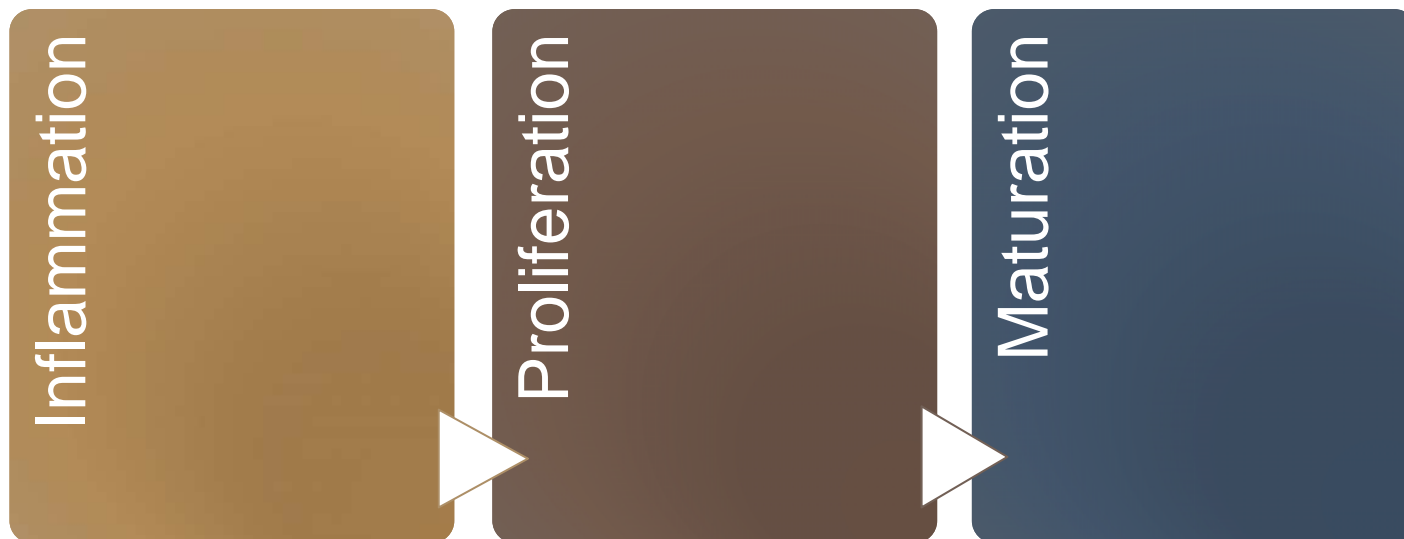
- pressure ulcers/injuries
- lower extremity ulcers
- diabetic foot ulcers
- venous ulcers and arterial ulcers



- Prevalence is measured by the number of cases of pressure ulcers at a specific time.
- Incidence measures the number of new pressure ulcers without an ulcer at baseline

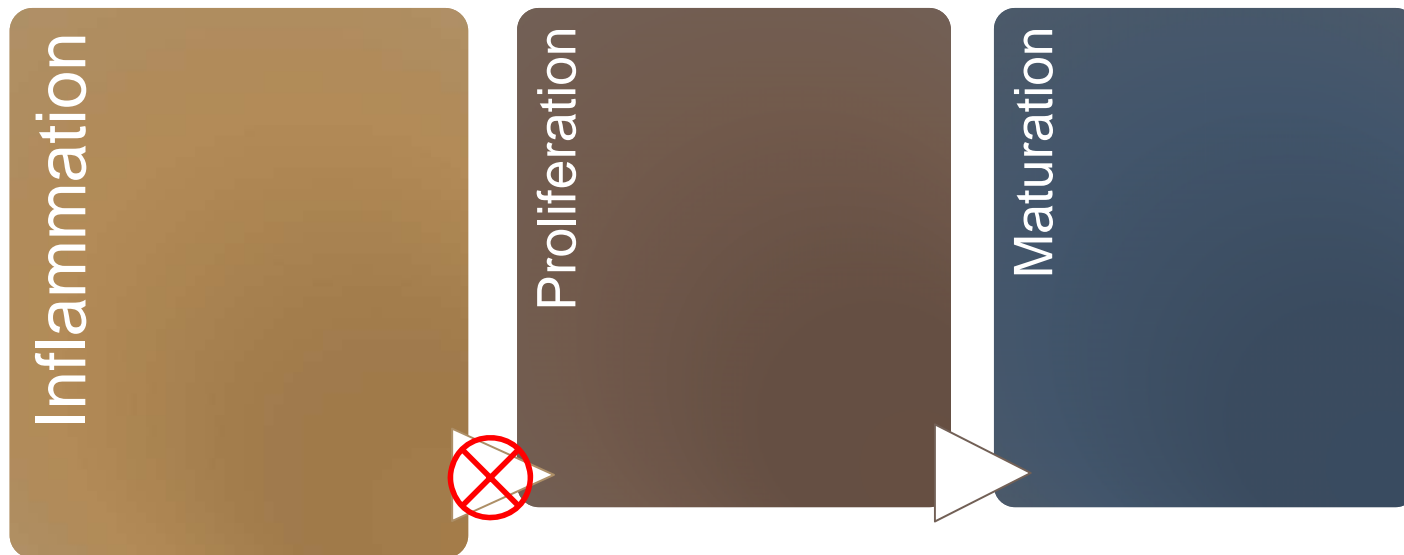
Healing Process for Wounds in Normal State

Three predictable, overlapping phases



Non-Healing, Chronic Wounds

Wounds get stuck in the inflammatory phase



AT RISK Patients: Common Factors



- Current or past medical condition(s) (eg, diabetes, renal disease, arterial disease)
- Immobility
- Incontinent
- Insufficient of sensory perception
- Compromised nutritional status (eg, malnutrition, dehydration, underweight, or overweight)

Wound Healing Elements

Nutrition/hydration is seen as one of the most modifiable factors affecting wound healing

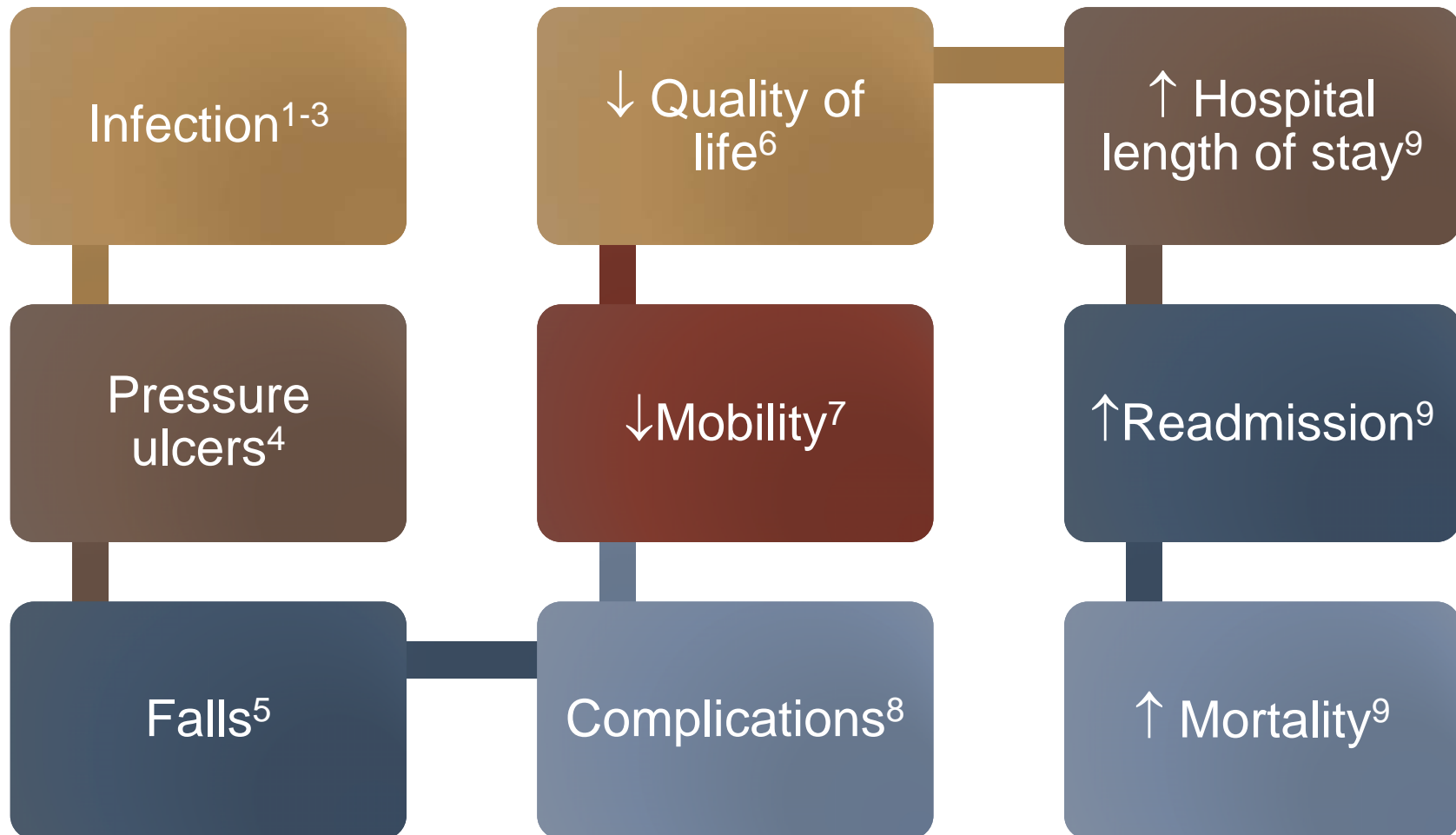
Extrinsic

- Mobility
- Wound bed environment
- Bacterial burden
- Soft tissue/bone infection
- Devitalized tissue
- Medications

Intrinsic

- Systemic disease
- Perfusion/oxygenation
- Infection process
- **Nutrition/hydration**
- Age

Malnutrition is a Significant Contributor to Adverse Outcomes



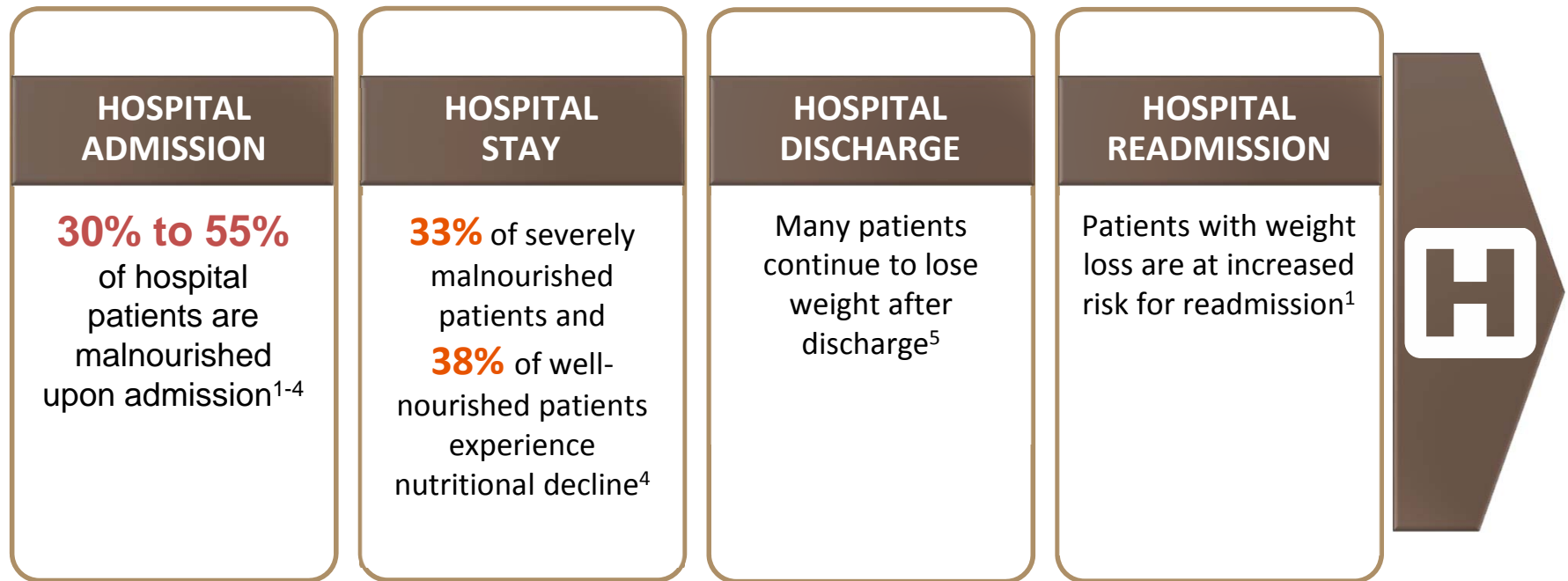
1. Schneider SM, et al. *Br J Nutr.* 2004;92:105-111. 2. Merli M, et al. *Clin Gastroenterol Hepatol.* 2010;8:979-985. 3. Lee S, et al. *Yonsei Med J.* 2003;44:203-209. 4. Fry D et al. *Arch Surg.* 2010;145:148-151; 5. Bauer JD et al. *J Nutr Diet.* 2007;20:558-564. 6. Kvamme JM, et al. *Qual Life Res.* 2010; 7. Vivanti A, et al. *J Nutr Health Aging.* 2011;15:388-391; 8. Sungurtekin H, *J Am Coll Nutr.* 2004;23:227-232; 9. Lim SL, et al. *Clin Nutr.* 2012;31(3):345-350.

Malnutrition Predicts Decubitus Ulcers

Malnutrition was the 3rd predictive factor for decubitus ulcers after major surgery

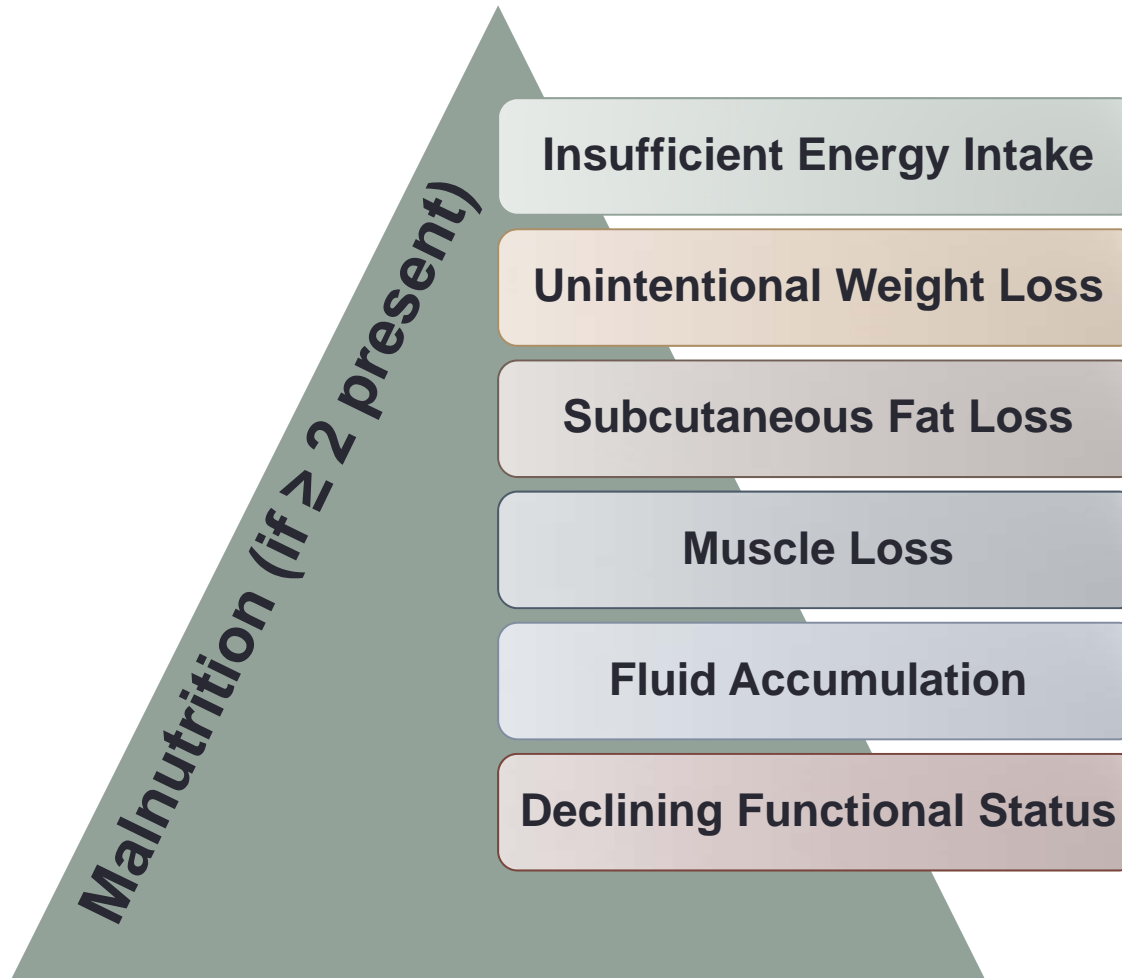
Preexisting Condition	Odds Ratio
Diabetic complications	5.3
Chronic renal failure	4.7
Malnutrition/weight loss	3.8
Peripheral vascular disease	2.3
Emergency admission	2.0

Prevalence of Malnutrition



1. Tappenden KA et al. *JPEN J Parenter Enteral Nutr.* 2013;37(4):482-497. 2. Naber TH et al. *Am J Clin Nutr.* 1997;66(5):1232-1239. 3. Somanchi M et al. *JPEN J Parenter Enteral Nutr.* 2011;35(2):209-216. 4. Braunschweig C et al. *J Am Diet Assoc.* 2000;100(11):1316-1322. 5. Beattie AH et al. *Gut.* 2000;46(6):813-818.

Use Multidisciplinary Team to Identify 6 Characteristics of Malnutrition



Loss of Muscle Mass & Function can Now Diagnose Malnutrition, Independent of Body Weight



NUTRIENT NEEDS

NPUAP Clinical Practice Guidelines: Evidence and Recommendations

JAN: RESEARCH METHODOLOGY: DISCUSSION PAPER – METHODOLOGY

The 2014 International Pressure Ulcer Guideline

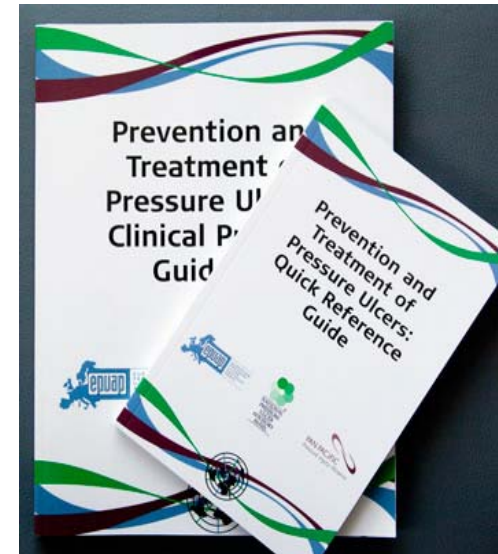
Table 4 Strengths of recommendations ratings.

Recommendation	Symbol	Description
Do it (Strong recommendation for using an intervention)	☺☺	Indicates a judgment that most well-informed people would make.
Do not do it (Strong recommendation against using an intervention)	☹☹	
Probably do it (Weak recommendation for using an intervention)	☺	Indicates a judgment that a majority of well-informed people would make, but a substantial minority would not.
Probably do not do it (Weak recommendation against using an intervention)	☹	
No specific recommendation	☹☺	Trade-offs between risk and benefit unclear or lack of agreement between voting participants

NPUAP Clinical Practice Guidelines for Energy Intake

“Offer fortified foods and/or high-calorie, high-protein oral nutritional supplements between meals if nutrition requirements cannot be achieved by dietary intake.”


- Strength of Evidence: B
- Strength of Recommendation: 👍 👍



NPUAP Clinical Practice Guidelines for Protein Intake

“Supplement with high protein, arginine, and micronutrients for adults with a pressure ulcer category/stage 3 or 4 or multiple pressure ulcers when nutritional requirements cannot be met with traditional high-calorie and protein supplements.”

Goal for protein support for patients with pressure ulcers

- 1.25-1.5 grams of protein per kilogram of body weight per day
- **Strength of Evidence: B**
- **Strength of Recommendation:** 

Carbohydrate

Glucose is the major fuel source for collagen synthesis and most efficient source of fuel compared with fat and protein.

- If insufficient CHO intake → the body breaks down protein to provide glucose for cellular activity.
 - Impaired utilization of CHO due to hyperglycemia leads to more proteolysis, glycogenolysis and lipolysis resulting in decreased wound healing
 - Hyperglycemia also leads to osmotic diuresis and loss of water and electrolytes which negatively impacts wound healing by decreasing tissue oxygenation
 - Both extracellular and intracellular dehydration occurs

Protein

Those with a protein malnutrition have a decreased immune system which places them at greater infection risk, leading to edema then, poor oxygenation of the tissue.

- The use of negative pressure wound therapy increases protein losses of an estimated 12.5 grams of protein per liter of fluid loss.

Protein Synthesis

Metabolic stress and catabolic states results in protein loss

- HMB activates of several signaling pathways that are important for protein translation
- Activation of protein translation helps to compensate for the loss of protein

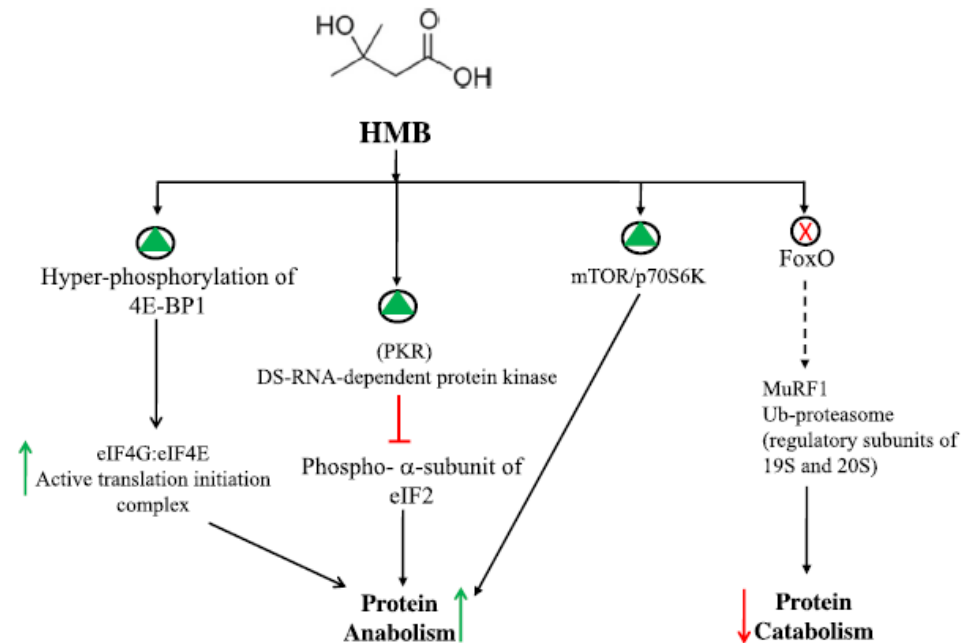
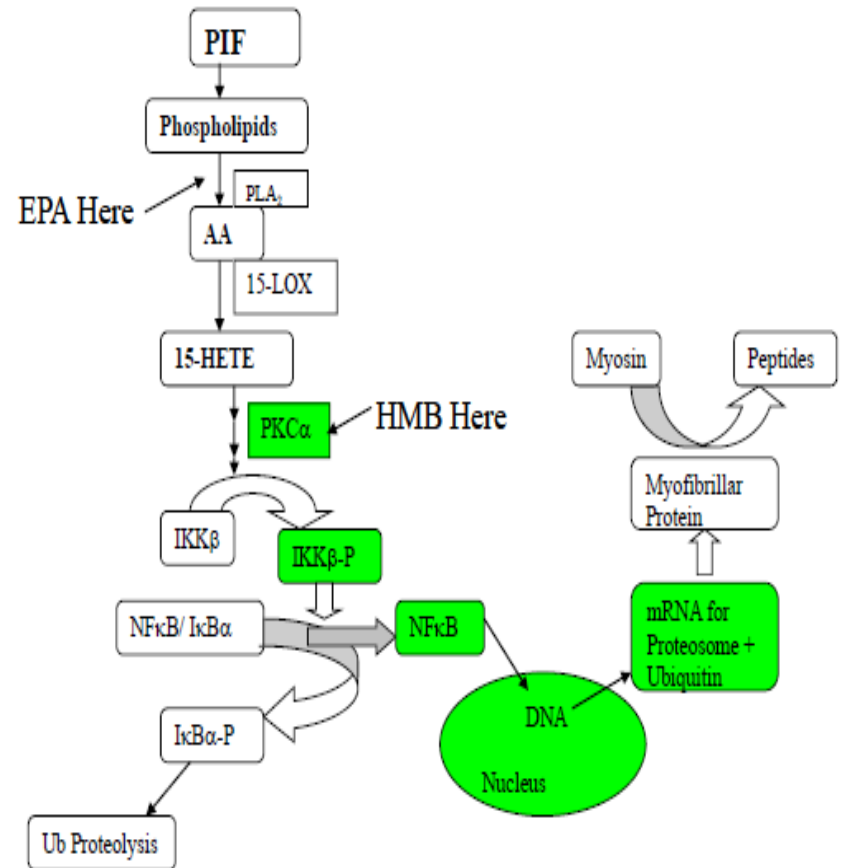


Fig. 3. Schematic representation of HMB therapeutic action in PIF/cancer/dexamethasone-induced atrophy.

Protein Degradation

One main pathway of protein degradation is via the ubiquitin-proteasome (Ub) pathway

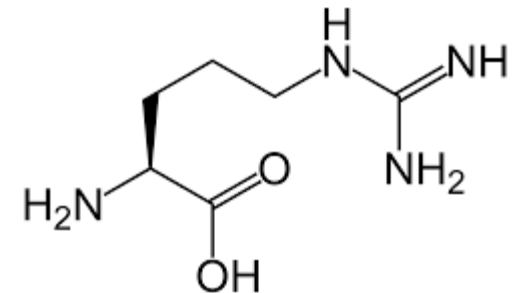
- Proteolysis inducing factor (PIF) can activate the Ub-pathway
- HMB has been shown block PIF induced activation of the Ub-pathway



Arginine

Considered a semi-essential amino acid

- Collagen and tissue synthesis require arginine for wound strength
- Nitric oxide is a product of arginine metabolism and is a powerful vasodilator that promotes angiogenesis (blood flow)
 - Beneficial in wound healing environment:
 - Toxic to bacteria
 - Inhibits platelet aggregation
 - Immune response mediator and neurotransmitter

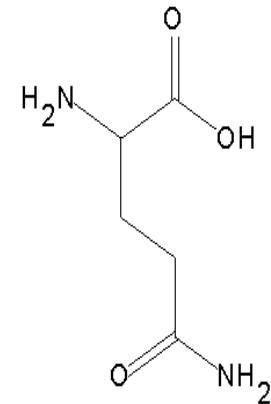


Studies have found that additional supplementation including arginine promotes wound healing in both nourished and malnourished patients

Glutamine

Serves as a fuel source for cells with rapid turnover such as enterocytes, epithelial cells, fibroblasts, macrophages and lymphocytes.

- Occurs in both inflammatory and proliferative phases of wound healing
- Essential for gluconeogenesis
- Demand increases during illness in the liver, kidney and GI tract
- No studies have been conducted on glutamine and wound healing for pressure ulcer patients.
 - *Neither the NPUAP nor the EPUAP recommend routine glutamine supplementation for pressure ulcers.*



Vitamin C

Antioxidant: cofactor in collagen formation and may help prevent wound infections by modulating immune function

Maintaining a balance between reactive oxygen species and anti-inflammatory substrates depends on optimal levels of vitamin C

Other studies on vitamin C do not support any positive effect on wound healing when supplemented with 1 g of vitamin C compared to those supplemented with 10 mg per day.

Vitamin E

Antioxidant

- Immune response and inflammation
 - Platelet aggregation, adhesion
 - Protein kinase C activation
 - Lipoprotein transport
 - Nucleic acid and protein metabolism
 - Mitochondrial function and hormonal production

Recent studies have shown a synergistic effect on pressure ulcer healing when combined with other antioxidants

- The other antioxidants included arginine and zinc as described.

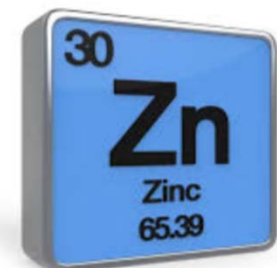
Zinc

Trace mineral with wide array of functions because of its presence as a component of several enzymes

- Co-factor for collagen and protein synthesis-*important for skin integrity and mucosal membranes*

Deficiency is associated with delayed wound healing

- Commonly seen in patients with diarrhea, malabsorption or hypermetabolic stress in sepsis, burns, or serious injury
- Poor zinc status can adversely affect B and T lymphocyte production, leading to delayed wound healing
- Supplementation without a deficiency has not been shown to be beneficial





NUTRITION SUPPLEMENTATION

Effect of Nutrition Supplements

Meta-analysis

- 4 RCTs
- *showed significantly lowered incidence of pressure ulcers among elderly hospitalized patients (OR 0.75) who used ONS (2-26 weeks) compared to non-users*

In-patient setting study

- *showed reduction of a prevalence rate of 7.8% to 1.4% upon utilization of evidence based criteria for the treatment of pressure ulcers.*

Assessing Changes in PU

- Pressure Ulcer Scale for Healing (PUSH)¹
- NPUAD tool to provide indications of improvement or deterioration in PU healing
- Assess size (LxW), exudate amount and tissue type
- Pressure Sore Status Tool (PSST)²
- Includes
 - Size, depth, edges, necrotic type, necrotic amount, exudate amount, skin color, edema, induration, granulation, epithelialization,
- Uses modified Likert scale (1 - healthiest to 5 - worst attribute)

1. <http://www.npuap.org/wp-content/uploads/2012/03/push3.pdf>

2. Bates-Jensen BM Adv Wound Care. 1997 Sep;10(5):65-73.

PUSH Tool 3.0

LENGTH X WIDTH (in cm ²)	0 0	1 < 0.3	2 0.3 – 0.6	3 0.7 – 1.0	4 1.1 – 2.0	5 2.1 – 3.0	Sub-score
		6 3.1 – 4.0	7 4.1 – 8.0	8 8.1 – 12.0	9 12.1 – 24.0	10 > 24.0	
EXUDATE AMOUNT	0 None	1 Light	2 Moderate	3 Heavy			Sub-score
TISSUE TYPE	0 Closed	1 Epithelial Tissue	2 Granulation Tissue	3 Slough	4 Necrotic Tissue		Sub-score
							TOTAL SCORE

TISSUE TYPE:

4 – Necrotic Tissue (Eschar): black, brown or tan tissue that adheres firmly to the wound bed or ulcer edges and may be either firmer or softer than surrounding skin

3 – Slough: yellow or white tissue that adheres to the ulcer bed in strings or thick clumps, or is mucinous

2 – Granulation Tissue: pink or beefy red tissue with a shiny, moist, granular appearance

1 – Epithelial Tissue: for superficial ulcers, new pink or shiny tissue (skin) that grows in from the edges or as islands on the ulcer surface

0 – Closed/Resurfaced: the wound is completely covered with epithelium (new skin)

Effect of Nutrition Supplements

Systematic review: arginine enriched nutrition

First author, year, country	Study design/duration	Setting	Patients' nutritional status	PU category	Age (years)	Sample size gender (M/F)	Interventions		Outcomes	Jadad scale
							Arginine group (N)	Control group (N)		
Cereda, 2015 ¹⁸ Italy	Multicentre blinded RCT, 8 weeks	Long-term care and home care services	Malnourished	II, III, or IV	81.4±10.7	200 (63/137)	Macronutrients with 1.5 g arginine (n=101)	Macronutrients without arginine (n=99)	PU area reduction, complete healing rate, wound infection rate, and dressings	6
Wong, 2014 ²³ Singapore	RCT, 2 weeks	Acute care hospital	Malnourished and non-malnourished	II, III, or IV	77.4±4.9	23 (9/14)	Standard oral nutritional supplements with 7 g arginine (n=11)	Standard oral nutritional supplements without arginine (n=12)	PU area, and PUSH score	6
Leigh, 2012 ²⁴ Australia	RCT, 3 weeks	Acute inpatient and rehabilitation services	Malnourished and well-nourished	II, III or IV	67.8±7.1	23 (11/13)	Standard hospital diet plus 4.5 g arginine (n=12)	Standard hospital diet plus 9 g arginine (n=11)	PUSH score	5
van Anholt, 2010 ²⁵ Europe	Multicountry, double-blind RCT, 8 weeks	Healthcare centres, hospitals, and long-term care facilities	Non-malnourished	III or IV	74.6±3.6	43 (19/24)	Oral nutritional supplements with 3 g arginine (n=22)	Oral nutritional supplements without arginine (n=21)	PU area, and PUSH score	5
Cereda, 2009 ²⁶ Italy	RCT, 12 weeks	Long-term care facility	NR	II, III, or IV	81.7±9.6	28 (10/18)	High-protein formula with 0.85 g arginine (n=13)	High-protein formula without arginine (n=15)	PUSH score, lesion area, nutritional variables, infection, occurrence, and hospitalisation	5
Desneves, 2005 ¹⁹ Australia	RCT, 3 weeks	Clinical setting	NR	II, III, or IV	73.2±10.9	16 (10/6)	Standard diet plus 9 g arginine (n=5)	Standard hospital diet or high-protein diet without arginine (n=11)	PUSH score	5
Benati, 2001 ²⁷ Italy	RCT, 2 weeks	Clinical setting	NR	PU's	72-91	16 (9/7)	Normal hospital diet plus 7.5 g arginine (n=6)	Normal hospital diet or high-protein calorie solution without arginine (n=10)	PSST score	4

Liu, P., et al (2017) *Journal of Wound Care*, 26(6), 319-323.

Effect of Nutrition Supplements

Systematic review: arginine enriched nutrition

7 RCTs with 369 patients;

- 4 RCTs assessed healing by PU area reduction
 - 1 enrolled malnourished patients
 - 1 enrolled non-malnourished patients
 - 2 studies did not restrict the nutritional status of the patients

Results:

- All reporting arginine-enriched enteral nutrition resulted in a significant PUSH score improvement compared with control at follow-up.
- An RCT compared healing with two doses of arginine (4.5g versus 9g), but no difference was found between the doses.

Effect of Nutrition Supplements

Systematic review: arginine enriched nutrition

- Evidence showed that arginine-enriched enteral nutrition led to a significant improvement in PU healing
- It was effective not only in malnourished patients, but also in non-malnourished patients

Suggest that arginine-enriched nutrition should be used in patients with pressure ulcers

Effect of Nutrition Supplements

Descriptive review: arginine enriched nutrition

Conducted in different settings: hospital, long-term care/care homes and home care.

- 7 RCTs
- 4 CTs
- Pressure ulcer stages II, III or IV

Results:

Ten out of eleven studies showed a beneficial effect of the arginine-enriched oral nutritional supplementation on the healing of pressure ulcers.

Effect of Nutrition Supplements

Descriptive review: arginine enriched nutrition

Characteristics of included studies.

1st Author	Follow-up	Sample size	Mean age (range)	PU-stage	Study type	Nutritional intervention serving/day, arginine/ONS	Comparison	Outcome measurement
Benati [24]	2 wks	N = 16	-(72-91)	-	RCT	specific ONS [⊖] , 2x, 3.75g	high-protein formula or normal hospital diet	PSST score
Frias Soriano [28]	3 wks	N = 39	75	III-IV	CT	specific ONS [⊖] , 2-3x, 3g	no ONS	complete healing/ PU area
Desneves [30]	3 wks	N = 16	73(37-92)	II-III-IV	RCT	specific ONS [⊖] , 2x, 9g	standard hospital diet or standard + protein-enriched ONS	PUSH score
Heyman [29]	9 wks	N = 245	82	II-III-IV	CT	specific ONS [⊖] , 1-3x, 3g	no ONS	complete healing/ PU area
Cereda [25]	12 wks	N = 10	82	II-III-IV	RCT	specific ONS [⊖] , 2x, 6g	standard hospital diet	PU area/ PUSH score
Brewer [32]	until healed	N = 35*	51	II-III-IV	CT	specific ONS [⊖] , 2x, 9g	no ONS (historical control)	healing rate/ time for closure
van Anholt [27]	8 wks	N = 43*	75	III-IV	RCT	specific ONS [⊖] , 1-3x, 3g	non-caloric control ONS	PU area/PUSH score, nursing time, number of dressings
Chapman [33]	until healed	N = 34	47	II-III-IV	CT	specific ONS [⊖] , 2x, 4.5g	ceased consuming specific ONS [⊖]	PUSH score
Leigh [31]	3 wks	N = 23*	(31-92)	II-III-IV	RCT	specific ONS ^{1⊖} , 1x, 4.5g specific ONS ^{2⊖} , 1x, 9.0g	standard hospital diet (historical control)	PU area/PUSH score/healing rate
Wong [34]	2 wks	N = 23	77	II-III-IV	RCT	specific ONS [⊖] , 2x, 7g	standard nutritional care	PU area/ PUSH score
Cereda [26]	8 wks	N = 200**	81	II-III-IV	RCT	specific ONS [⊖] , 2x, 6g	isocaloric, isonitrogenous ONS	complete healing/ PU area

Effect of Nutrition Supplements

The OligoElement Sore Trial

Patients

- Malnourished
- 200 patients
- II, III, or IV pressure ulcers

Intervention

- 400ml/d x 8 weeks
- Energy dense, protein rich
- Zinc & Arginine

Effect of Nutrition Supplements

The OligoElement Sore Trial

Both groups



- 2 bottles per day
- 500 kcals
- 40g protein

Intervention



- Zinc
- Vitamin E
- Vitamin C

Effect of Nutrition Supplements

The OligoElement Sore Trial

END POINTS	Experimental Group (n=101)	Control Group (N=99)	P Value
Primary			
Mean reduction in PU area at 8 wk, %	60.9 (54.3 to 67.5)	45.2 (38.4 to 52.0)	0.026*
Secondary			
≥40% reduction in PU area at 8wk, %	69.9 (59.5 to 79.9)	54.1 (42.7 to 65.5)	0.020*
Complete Healing, %	16.9 (8.2 to 25.6)	9.7 (2.1 to 17.3)	0.100
Mean reduction in PU area at 4 wk, %	37.2 (28.7 to 45.8)	29.3 (21.9 to 36.7)	0.25
Wound Infections, %	22.6 (11.8 to 33.2)	21.6 (12.0 to 31.1)	0.88
Mean dressings, n	34 (30 to 80)	37 (34 to 41)	0.32

Effect of Nutrition Supplements

The OligoElement Sore Trial

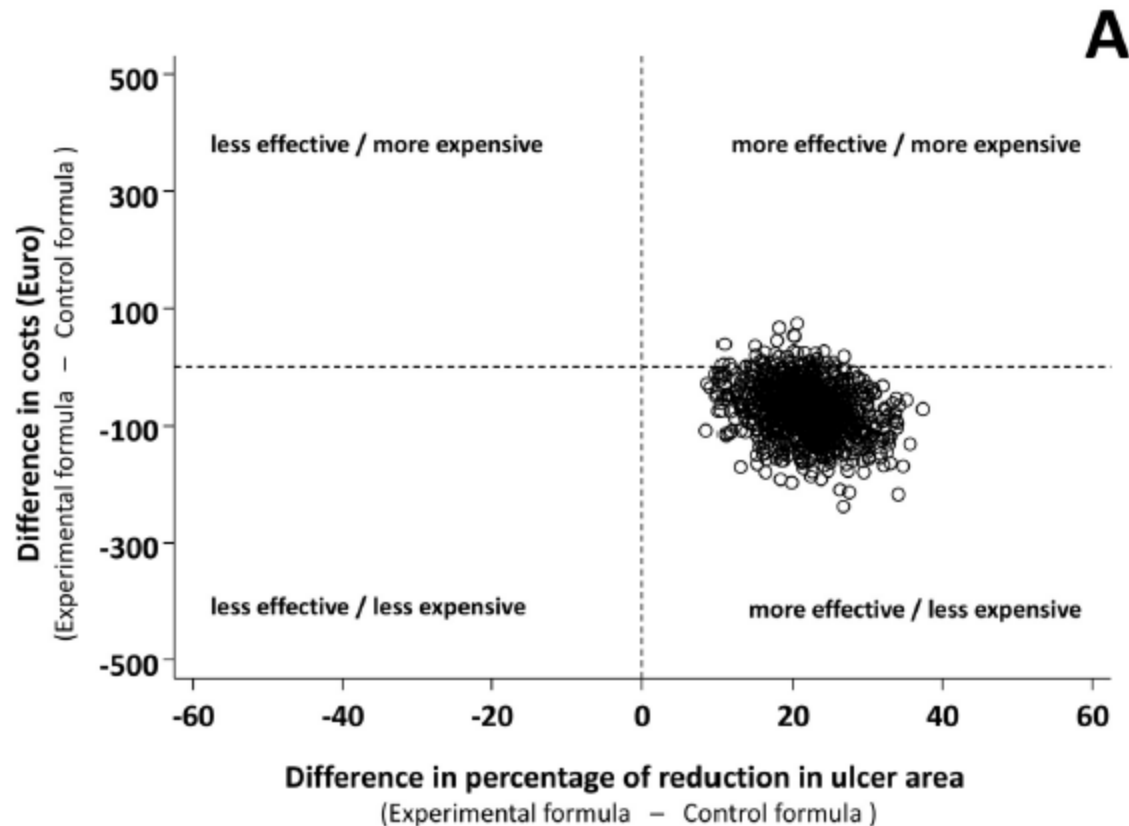
RESULTS:

- Supplementation with the enriched formula (n = 101) resulted in a greater reduction in PU area (mean reduction, 60.9% [95% CI, 54.3% to 67.5%]) than with the control formula (n = 99) (45.2% [CI, 38.4% to 52.0%]) (adjusted mean difference, 18.7% [CI, 5.7% to 31.8%])
- The secondary outcome saw a 40% or greater reduction in pressure ulcer size in the experimental group compared to control group that was significant
- No difference was found in other secondary end points. The level of significance was set at the 2-tailed P value less than 0.05.

Overall treatment was effective in improving pressure ulcer healing

Effect of Nutrition Supplements

The OligoElement Sore Trial





SUMMARY

Summary

- Studies suggest the efficacy of nutrients in wound healing is likely synergistic as there is lack of evidence supporting an independent effect when the supplemented nutrients are given alone.
- Intervention studies have led to the recommendation of supplements enriched with protein, arginine, and micronutrients for stage III and IV when traditional nutrition therapy does not meet nutrient requirements

Summary



- Supplementation seems to be associated with a significant reduction in pressure ulcer development, compared to routine care.
- Oral nutrition supplementation is valuable because many pressure-ulcer-prone patients often cannot meet their nutritional requirements via normal food intake.
- Offering a high-protein mixed oral nutritional supplement in addition to the usual diet to individuals with nutritional risk and pressure ulcer risk can be beneficial.

<https://www.surveymonkey.com/r/WoundCE>



QUESTIONS?
